M

## WHAT IS CLAIMED IS:

1. A method for the preparation of a substance selected from the group comprising the fibrates corresponding to the general formula:

TO190 X

$$R_{1} = \begin{pmatrix} CH_{3} \\ I \\ O-C-C \\ O-R_{2} \end{pmatrix}$$
 (I)

PS H

in which  $R_1$  represents especially a halogen atom (in particular F, Cl or Br, the preferred halogen atom being Cl) or an acetyl, (4-chlorophenyl)hydroxymethyl, 4-chlorobenzoyl or 2-(4-chlorobenzamido)ethyl group and  $R_2$  represents a  $C_1$ - $C_4$  alkyl group in which the hydrocarbon chain is linear or branched, which comprises reacting an excess, relative to the stoichiometric conditions, of an alkyl 2-bromo-2-methylpropanoate of the formula:

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$$\begin{array}{ccc}
& & \text{CH}_3 & \text{O} \\
& & \text{Br-C-C} & \\
& & \text{CH}_3 & \text{O} & \\
\end{array}$$

70191X

in which  $\mathbf{R}_2$  is defined as indicated above, with a substituted phenol of the formula:

r0192 X

$$R_1$$
—OH (VI)

PS H

in which  $\mathbf{R}_1$  is defined as indicated above, in the absence of a solvent and in the presence of an excess of

19

 ${\rm K_2CO_3}$ , relative to the stoichiometric conditions, at a temperature greater than or equal to 120°C, for at least 2 h.

- 2. The method according to claim 1, wherein the resulting fibrate is isolated from the reaction medium by precipitation, extraction or distillation.
- 3. The method according to claim 1, wherein the reaction medium containing the resulting fibrate is treated with a strong acid to neutralize the excess  $K_2^{\text{CO}}_3$ , and the fibrate is then isolated from the reaction medium by precipitation, extraction or distillation.
- 4. The method according to claim 1, wherein 1 mol of VI is reacted with about 1.7 to about 2.3 mol of V in the presence of about 0.8 to about 1.8 mol of  $\rm K_2CO_3$ , at a temperature of 120 to 160°C, for 3 to 6 hours.
- 5. The method according to claim 1, wherein 1 mol of VI is reacted with about 2 mol of V in the presence of about 1 mol of  $K_2CO_3$ , at a temperature of 140 to 145°C.
- 6. The method according to claim 3, wherein the neutralization of the excess  $K_2^{CO}$  is carried out with sulfuric acid at a temperature not exceeding 120°C and preferably of the order of 100°C.
- 7. The method according to claim 1, wherein:
- $1^{\sqrt{1}}$ ) about one mol of VI is reacted with about 1.7 to about 2.3 mol of V (preferably about 2 mol of V) in the absence of a solvent and in the presence of about 0.8 to about 1.8 mol of  $K_2^{CO}$  (preferably about 1 mol of  $K_2^{CO}$ ), at a temperature of 120°C to 160°C (preferably at a temperature of 140°C to 145°C), for at least 2 hours (preferably for 3 to 6 hours),
- $_{\text{A}}\text{2}^{\text{O}})$  the excess  $\text{K}_{2}\text{CO}_{3}$  is neutralized with a strong acid at a temperature below 120°C, and
- $3^{\varrho^3}$ ) the fibrate is isolated from the reaction medium by precipitation at a temperature below 60°C, or by extraction or distillation.

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- 8. The method according to claim 1 for the preparation of fenofibrate, wherein:
- (a) about 1 mol of VI in which  $R_1$  is the 4-chlorobenzoyl group is reacted with about 2 mol of V in which  $R_2$  is the isopropyl group, in the absence of a solvent and in the presence of about 1 mol of  $K_2^{CO}_3$ , at a temperature of about 140°C to about 145°C, for about 5 hours,
- (b) after the addition of aqueous isopropanol to the resulting reaction medium, the excess  $K_2^{CO}_3$  is neutralized with sulfuric acid at a temperature of the order of  $100^{\circ}C$ .
- (c) the resulting reaction medium is cooled to a temperature of between 15 and 25°C and the precipitate of fenofibrate is collected by filtration,
- (d) the precipitate filtered off in this way is washed with sodium hydroxide followed by water, and then
- (e) the fenofibrate is recrystallized from aqueous isopropanol.
- 9. The method of preparation according to claim 1 for the synthesis of a fibrate of the formula I in which  $R_2$  = H, wherein the corresponding ester is prepared, according to the method of claim 1, by reacting the substituted phenol VI with an alkyl 2-bromo-2-methyl-propanoate of the formula V in which  $R_2$  is a  $C_1$ - $C_4$  alkyl group, in the absence of a solvent, and the resulting ester is then saponified.

end\_\_\_

Pi 14

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Pi H

Y<sub>1</sub>

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